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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/593,223	09/17/2007	Matthias Boy	BGI-191US	7042
959 7590 08/20/2008 LAHIVE & COCKFIELD, LLP FLOOR 30, SUITE 3000 ONE POST OFFICE SQUARE BOSTON, MA 02109				
EXAMINER GOON, SCARLETT Y				
ART UNIT		PAPER NUMBER		
1623				
MAIL DATE		DELIVERY MODE		
08/20/2008		PAPER		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/593,223

Applicant(s)

BOY ET AL.

Examiner

SCARLETT GOON

Art Unit

1623

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 September 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3-7 and 9-22 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3-7 and 9-22 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/5508)
Paper No(s)/Mail Date 17 September 2007.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____.
- 5) ☐ Notice of Informal Patent Application.
- 6) ☐ Other: _____.

DETAILED ACTION

The preliminary amendment filed on 17 September 2007 in which claims 2 and 8 were cancelled, claims 1, 3-7 and 9-12 were currently amended, and claims 13-22 were newly added, is acknowledged.

Claims 1, 3-7 and 9-22 are pending in the instant application.

Priority

This application is a National Stage entry of PCT/EP05/02936 filed on 18 March 2005 and claims priority to Germany foreign application 10 2004 013 736.6 filed on 18 March 2004. A certified copy of the foreign priority document in German has been received. No English translation has been received.

Information Disclosure Statement

The information disclosure statement (IDS) dated 17 September 2007 complies with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609. Accordingly, it has been placed in the application file and the information therein has been considered as to the merits.

Specification

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: Methods for the Enrichment of Trehalose Using Zeolites.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

[Section 0001]

Claims 1, 3, 5, 6 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 6,200,783 B1 to Chaen *et al.* (herein referred to as the '783 patent, PTO-892, Ref. A) and PG Pub No. US 2003/0222021 A1 by Ennelin *et al.* (PTO-892, Ref. B).

The Chaen '783 patent teaches a process for separating trehalose and/or sugar alcohols from hydrogenated saccharide mixtures containing trehalose and sugar alcohols. Trehalose is a non-reducing disaccharide composed of two glucose molecules bound at their reducing groups. It is more stable than sucrose and can be used as a sweetener. It is now sought after as a sucrose substitute in the fields of foods, cosmetics, and pharmaceutical industries (column 1, lines 15-21). One method of obtaining trehalose is from enzymatic synthesis, using maltose as a substrate (column 1, lines 33-36). The enzymatic reaction is an equilibrium reaction, therefore resulting in a mixture of maltose and trehalose (column 1, lines 37-39). In order to easily separate the mixture using chromatographic techniques, the reaction is hydrogenated, thereby reducing unreacted maltose to maltitol, but leaving trehalose unaltered (column 1, lines 60-66). The mixture can then be purified using strong-acid cation exchange resins, which easily separates trehalose from the hydrogenated saccharide mixtures (column 2, lines 36-38). Examples of resins suitable for separation of the reaction mixture are those that belong to the family of strong-acid cation exchange resins, such as styrene/divinylbenzene polymers with a cross-linking of 2-8% (column 4, lines 51-58). Water is used as the

elution buffer (moving bed) in the column chromatography (column 5, lines 6-7) and the various fractions are collected. Fractions rich in trehalose are the first to elute, followed by fractions rich in sugar alcohols (column 5, lines 34-36). If necessary, the resulting fractions can be further treated with conventional filtration, centrifugation, decoloration, desalting, concentration, crystallization, separation, drying, pulverizing, and/or cutting to obtain the desired trehalose (column 5, lines 40-44).

The Chaen '783 patent does not explicitly teach a method wherein the resin used in chromatography is zeolite.

Ennelin *et al.* teach a chromatographic separation process of recovering mannose with high purity. The chromatographic separation for obtaining mannose is typically carried out with a strongly acidic cation exchange resin (paragraph 0046). A preferred resin is a cross-linked styrene-divinylbenzene based resin with cross-linking of 3-8%. Alternatively, zeolite-based molecular sieves can be used (paragraph 0046). The eluant used in the chromatographic separation is either water or a solvent, or mixture thereof (paragraph 0047). The chromatographic separation method may further comprise one or more purification steps selected from membrane filtration, ion exchange, evaporation, filtration and derivatization (paragraph 0051). These purification steps may be carried out before or after the chromatographic separation.

It is noted that the references do not explicitly teach the limitation of claim 3 wherein the trehalose is adsorbed onto the zeolite. However, one of ordinary skill in the art is well aware that purification by column chromatography works due to the differing interactions (or adsorption) each substance has with the resin or molecular sieve.

Therefore, since the Chaen '783 patent does teach that trehalose is purified by strong acid cation exchange resin, it is *prima facie* obvious that the compound is adsorbed onto the resin.

As such, it would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of the Chaen '783 patent, concerning the purification of trehalose using a strong-acid cation-exchange resin, with the teachings of Ennelin *et al.*, regarding the purification of sugars using strong-acid cation-exchange resins or zeolite . As both the Chaen '783 patent and Ennelin *et al.* teach the use of similar strong-acid cation-exchange resins in the purification of their respective sugars, cross-linked styrene-divinylbenzene based resin with cross-linking of 3-8%, and Ennelin *et al.* further teach that zeolite can also be used for purification of the sugars, suggesting that zeolite is equivalent to cross-linked styrene-divinylbenzene based resin with cross-linking of 3-8%, it would have been *prima facie* obvious to one of ordinary skill in the art that zeolite is also a feasible option for use in the purification of trehalose. One of ordinary skill in the art would fully appreciate knowing what other alternatives are available for use, providing one with a greater choice for selection, particularly if one reagent unexpectedly becomes unavailable.

Thus, the claimed invention as a whole is *prima facie* obvious over the combined teachings of the prior art.

[Section 0002]

Claims 4 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 6,200,783 B1 to Chaen *et al.* (herein referred to as the '783 patent, PTO-892, Ref. A) and PG Pub No. US 2003/0222021 A1 by Ennelin *et al.* (PTO-892, Ref. B) as applied to claims 1, 3, 5, 6 and 19 above, and further in view of PG Pub No. US 2005/0202139 A1 to Corbin *et al.* (PTO-892, Ref. C).

The teachings of the Chaen '783 patent and Ennelin *et al.* were as described above in section [0001] of the claim rejection under 35 USC § 103.

The references do not explicitly teach a method wherein the zeolite is selected from the group consisting of FAU, BEA, DON, EMT, CFI, MOR, MAZ and OFF.

Corbin *et al.* teach a process for using a zeolite or zeolite molecular sieves for recovering isoflavones from aqueous mixtures. The zeolite framework structure has corner-linked tetrahedral with Al or Si atoms at centers of the tetrahedral and oxygen atoms at the corners (paragraph 0059). Such tetrahedral are combined in a well-defined repeating structure comprising various combinations of 4-, 6-, 8-, 10- and 12-membered rings. The resulting framework structure is a pore network of regular channels and cages that is useful for separation. Pore dimensions are determined by the geometry of the aluminosilicate tetrahedral forming the zeolite channels or cages. Pore dimensions are critical to the performance of these materials in catalytic and separation applications, since this characteristic determines whether molecules of a certain size can enter and exit the zeolite framework (paragraph 0059). In practice, it has been observed that very slight decreases in ring dimensions can effectively hinder or block movement of particular molecular species through the zeolite structure. The

effective pore dimensions that control access to the interior of the zeolites are determined not only by the geometric dimensions of the tetrahedral forming the pore opening, but also by the presence or absence of ions in or near the pore (paragraph 0060). Representative examples of zeolites are (i) small pore zeolites such as NaA (LTA), CaA 9LTA), Erionite, (ERI), Rho (RHO), ZK-5 (KFI) and chabazite (CHA); (ii) medium pore zeolites such as ZSM-5 (MFI), ZSM-11 (MEL), ZSM-22 (TON), and ZSM - 48; and (iii) large pore zeolites such as zeolite beta (BEA), faujasite (FAU), mordenite (MOR), zeolite L (LTL), NaX (FAU), NaY (FAU), DA-Y (FAU) and CaY (FAU) (paragraph 0062). The letters in parentheses give the framework structure type of the zeolite.

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of the Chaen '783 patent, concerning the purification of trehalose using a strong-acid cation-exchange resin, with the teachings of Ennelin *et al.*, regarding the purification of sugars using strong-acid cation-exchange resins or zeolite, with the teachings of Corbin *et al.*, regarding the zeolite framework structure and the criticality of the pore dimensions to the performance of zeolites in separation applications. It would have been *prima facie* obvious that one of ordinary skill in the art would be aware of the various types of zeolites available, as well as their properties, such as the different pore dimensions. Therefore, depending on the materials one is interested in separating, it would have been *prima facie* obvious that one of ordinary skill in the art would know how to select the proper zeolite most suitable for the separation of their desired materials.

Thus, the claimed invention as a whole is *prima facie* obvious over the combined teachings of the prior art.

[Section 0003]

Claims 7, 9, 10, 12, 13 and 16-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 6,200,783 B1 to Chaen *et al.* (herein referred to as the '783 patent, PTO-892, Ref. A), US Patent No. 5,441,644 to Kinouchi (herein referred to as the '644 patent, PTO-892, Ref. D), and PG Pub No. US 2003/0222021 A1 by Ennelin *et al.* (PTO-892, Ref. B).

The teachings of the Chaen '783 patent were as described above in section [0001] of the claim rejection under 35 USC § 103.

The reference does not explicitly teach a method wherein trehalose is enriched from a fermentation broth, nor does the reference teach a method wherein the resin used in chromatography is zeolite.

The Kinouchi '644 patent teaches a method for isolating and purifying trehalose from trehalose-containing solutions. The origin of the trehalose-containing solution to be processed is not limited. For example, the trehalose solutions could have been obtained as intermediates in various processes of producing, extracting, etc., trehalose from natural substances such as a dry yeast; various aqueous trehalose solutions obtained as intermediates in various processes of obtaining trehalose by enzymatically converting maltose, sucrose or the like into trehalose; and various trehalose solutions obtained as intermediates in processes of obtaining trehalose by culturing

microorganisms (column 3, lines 8-20). The processes of producing trehalose by culturing microorganisms may be any such known process that utilizes known microorganisms of the genera Nocardia, Rhizoctonia and Sklerotium. Other aqueous solutions derived from fermentation liquids obtained from culturing microorganisms belonging to the genus Brevibacterium, Corynebacterium, Microbacterium or Arthrobacter may also be used (column 3, lines 21-34). When the trehalose solutions are derived from culturing microorganisms, the cells are removed from the culture liquid, the culture liquid is then treated with methanol, and the insoluble substances are removed by filtration (column 2, lines 1-4). The trehalose can then be isolated from the filtrate by first subjecting a trehalose-containing solution to ultrafiltration, preferably with an ultrafilter, and then concentrating and preferably cooling the solution to crystallize trehalose dehydrate in and from the trehalose-containing solution so as to obtain highly-pure crystals of trehalose dehydrate in high yield (column 3, lines 1-7).

The teachings of Ennelin *et al.* were as described above in section [0001] of the claim rejection under 35 USC § 103.

It is noted that the references do not explicitly teach the limitation of claim 13 wherein the trehalose is adsorbed onto the zeolite. However, one of ordinary skill in the art is well aware that purification by column chromatography works due to the differing interactions (or adsorption) each substance has with the resin. Therefore, since the Chaen '783 patent does teach that trehalose is purified by strong acid cation exchange resin, it is *prima facie* obvious that the compound is adsorbed onto the resin.

It is noted that the references do not explicitly teach the separation of an additional product, as listed in instant claim 18, from the fermentation broth. However, the Kinouchi '644 patent does teach that after removal of the cells, the culture liquid is then treated with methanol, and the insoluble substances are removed by filtration (column 2, lines 1-4). The addition of methanol to a cell culture, or solution, is known to precipitate out proteins, peptides and polysaccharides (see EP 0251727, p. 4, paragraph 10, PTO-892, Ref. N).

As such, it would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of the Chaen '783 patent, concerning the purification of trehalose using a strong-acid cation-exchange resin, with the teachings of the Kinouchi '644 patent, regarding a method for isolating and purifying trehalose from trehalose-containing solutions derived from various sources, with the teachings of Ennelin *et al.*, regarding the purification of sugars using strong-acid cation-exchange resins or zeolite. As both the Chaen '783 patent and Ennelin *et al.* teach the use of similar strong-acid cation-exchange resins in the purification of their respective sugars, cross-linked styrene-divinylbenzene based resin with cross-linking of 3-8%, and Ennelin *et al.* further teaches that zeolite can also be used for purification of the sugars, suggesting that zeolite is equivalent to cross-linked styrene-divinylbenzene based resin with cross-linking of 3-8%, it would have been *prima facie* obvious to one of ordinary skill in the art that zeolite is also a feasible option for use in the purification of trehalose. One of ordinary skill in the art would fully appreciate knowing what other alternatives are available for use, providing one with a greater choice for selection, particularly if one

reagent unexpectedly becomes unavailable. Furthermore, it is *prima facie* obvious that the only requirement for purification of trehalose by strong-acid cation-exchange resin or zeolite chromatography is that the trehalose is present as an aqueous solution. Thus, one can purify trehalose obtained from any known number of sources, including enzymatic and cultured microorganisms.

Thus, the claimed invention as a whole is *prima facie* obvious over the combined teachings of the prior art.

[Section 0004]

Claims 11, 14, 15 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 6,200,783 B1 to Chaen *et al.* (herein referred to as the '783 patent, PTO-892, Ref. A), US Patent No. 5,441,644 to Kinouchi (herein referred to as the '644 patent, PTO-892, Ref. D), and PG Pub No. US 2003/0222021 A1 by Ennelin *et al.* (PTO-892, Ref. B) as applied to claims 7, 9, 10, 12, 13 and 16-18 and further in view of PG Pub No. US 2005/0202139 A1 to Corbin *et al.* (PTO-892, Ref. C).

The teachings of the Chaen '783 patent and Ennelin *et al.* were as described above in section [0001] of the claim rejection under 35 USC § 103. The teachings of the Kinouchi '644 patent were as described above in section [0003] of the claim rejection under 35 USC § 103

The references do not explicitly teach a method wherein the zeolite is selected from the group consisting of FAU, BEA, DON, EMT, CFI, MOR, MAZ and OFF.

The teachings of Corbin *et al.* were as described above in section [0002] of the claim rejection under 35 USC § 103.

With respect to instant claims 11 and 22 wherein the trehalose is present in the fermentation broth at a concentration of less than 15 percent by weight, it is noted that the references do not explicitly teach this limitation. However, one of ordinary skill in the art would be aware that the concentration of trehalose present in a fermentation broth can be adjusted by altering the growth conditions of the microorganism, such as time of growth, cell density, temperature, etc.

As such, it would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of the Chaen '783 patent, concerning the purification of trehalose using a strong-acid cation-exchange resin, with the teachings of the Kinouchi '644 patent, regarding method for isolating and purifying trehalose from trehalose-containing solutions derived from various sources, with the teachings of Ennelin *et al.*, regarding the purification of sugars using strong-acid cation-exchange resins or zeolite, with the teachings of Corbin *et al.*, regarding the zeolite framework structure and the criticality of the pore dimensions to the performance of zeolites in separation applications. It is *prima facie* obvious that one of ordinary skill in the art would be aware of the various types of zeolites available, as well as their properties, such as the different pore dimensions. Therefore, depending on the materials one is interested in separating, it would have been *prima facie* obvious that one of ordinary skill in the art would know how to select the proper zeolite most suitable for the separation of their desired materials.

Thus, the claimed invention as a whole is *prima facie* obvious over the combined teachings of the prior art.

[Section 0005]

Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 6,200,783 B1 to Chaen *et al.* (herein referred to as the '783 patent, PTO-892, Ref. A) and PG Pub No. US 2003/0222021 A1 by Ennelin *et al.* (PTO-892, Ref. B) as applied to claims 1, 3, 5, 6 and 19 above, and further in view of US Patent No. 5,441,644 to Kinouchi (herein referred to as the '644 patent, PTO-892, Ref. D).

The teachings of the Chaen '783 patent and Ennelin *et al.* were as described above in section [0001] of the claim rejection under 35 USC § 103.

The Chaen '783 patent specifically teaches that the resulting trehalose fractions eluted from the chromatography column can be further treated with conventional filtration, centrifugation, decoloration, desalting, concentration, crystallization, separation, drying, pulverizing, and/or cutting to obtain the desired trehalose (column 5, lines 40-44). However, the references do not explicitly teach that the filtration technique involves ultrafiltration.

The teachings of the Kinouchi '644 patent were as described above in section [0003] of the claim rejection under 35 USC § 103.

As such, it would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of the Chaen '783 patent, concerning the purification of trehalose using a strong-acid cation-exchange resin, with the teachings of

Ennelin *et al.*, regarding the purification of sugars using strong-acid cation-exchange resins or zeolite, with the teachings of the Kinouchi '644 patent, regarding a method for isolating and purifying trehalose from trehalose-containing solutions that includes the step of ultrafiltration. It is *prima facie* obvious that one of ordinary skill in the art would know of the various filtration techniques available to them, and therefore decide which technique would be most suitable for their purposes of further purifying trehalose to remove any impurities that may have eluted with the compound during column chromatography.

Thus, the claimed invention as a whole is *prima facie* obvious over the combined teachings of the prior art.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SCARLETT GOON whose telephone number is 571-270-5241. The examiner can normally be reached on Mon - Thu 7:00 am - 4 pm and every other Fri 7:00 am - 12 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for

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/Shaojia Anna Jiang, Ph.D./
Supervisory Patent Examiner, Art Unit 1623

/SCARLETT GOON/
Examiner
Art Unit 1623